titanium surface by APTES silanization is an effective approach to prevent bacterial infection in vivo.
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IN VIVO EVALUATION OF THE ANTI-INFECTION POTENTIAL OF GENTAMICIN-LOADED NANOTUBES ON TITANIA IMPLANTS

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Introduction: Currently, implant-associated infection is one of the critical causes of implant failures in orthopedic surgery. Titanium and titanium alloys are the most widely used implant materials and have good biocompatibility and excellent mechanical properties. However, these implant surfaces also favor bacterial adhesion, colonization and biofilm formation, and there is competition of initial adhesion to the implant surface between bacteria and osteoprogenitors. Therefore, good antibacterial properties and osteoblast activity are the key points involved in implant material manufacturing.
Subjects and Methods: Thirty-six male Sprague-Dawley (SD) rats were used to establish an implant-associated infection model. A volume of 50 μl *Staphylococcus aureus* suspension (1×10^5 CFUs/ml) was injected into the medullary cavity of the left femur, and then the titanium rods without modification (Ti), titanium nanotubes without drug-loading (NT) and gentamicin-loaded titanium nanotubes (NT-G) were inserted with PBS-inoculated Ti rods as a blank control. X-ray images were obtained 1, 21, and 42 days after surgery, micro-CT, microbiological and histopathological analysis were used to evaluate the infections at the time of sacrifice.
Results: Radiographic signs of bone infection, including osteolysis, periosteal reaction, osteosclerosis and damaged articular surfaces were demonstrated in the infected Ti group and were slightly alleviated in the NT group, but not observed in the NT-G group. Meanwhile, the radiographic and gross bone pathological scores of the NT-G group were significantly lower than those of the infected Ti group (live bacterial growth compared with the Ti group; *p* confirmed decreased bacterial burden in the NT-G group compared with the Ti and NT groups).
Discussion and Conclusion: The traditional remedy of an infected implant is a prolonged systemic antibiotic administration after device removal. The local use of antibiotic-loaded nanotubes has been widely reported to prevent this intractable clinical condition experimentally. Meanwhile, nanostructured surface topographies have been explored as effective approaches for enhancing desirable osteogenesis. Our previous research has demonstrated that gentamicin-loaded nanotubes with diameters of 80 nm exhibited predictable drug release kinetics and significantly improved antimicrobial activity. In this study, we further investigated the effectiveness of gentamicin-loaded nanotubes on titanium surfaces to prevent implant-associated infections in a rat model. In general, this effective *in vivo* study showed that the NT-G group exhibited significant bacterial inhibition when compared with the Ti and NT groups in this *S. aureus* infection rat model. The NT coatings also resulted in alleviated bacterial burdens, and therefore demonstrated the feasibility of the clinical application of this antibiotic-loaded titanium nanotube-based implant for combating orthopedic implant-associated infection.
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A NOVEL FIXATIVE NEEDLE CARRIED Mg CAN PROMOTE FRACTURE HEALING IN OVX RATS

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Introduction: Magnesium (Mg) can promote the new bone formation in the periosteum region after intramedullary implanted into the rat femur canal. This osteogenic effect inspired us to apply it into the OVX rat fracture healing. Mg itself is too soft to fix the rat fracture bone directly, that puzzled clinicians without a resolution of enhancing Mg metal's strength. Here we designed a novel fixative needle-encapsulated Mg intramedullary nail to fixate the fractured bone. We speculated Mg ions which released through the window at middle site of the needle can promoted the fracture healing. That will make Mg's orthopedic application into an applicable real.
Methods: Three kinds of needle designs were drafted in software SolidWorks. Finite elemental analysis (FEA) was used to screen design drawing with the best mechanical performance and broad window area. 18G spinal needles were machined as rough blank. Mg degradation captured in designed needle was evaluated in vitro. 48 3-month old rats were ovariectomized and raised to 9-month old to perform osteoporosis. Then rats were made to closed fracture on right femur and fixed separately by designed needle ($n = 24$) and blank needle ($n = 24$). Samples were harvested at week 2, 4, 8, 12 (all groups with 6 samples at each time point). Micro-CT scanning and X-ray photographs were applied to analyse fracture callus. Samples at week 12 were under mechanical test. Callus area and length in X-ray results, callus total volume and bone volume, callus bone density, mechanical strength and E-modulus were analysed.
Results: The window design was evolved from original semi-roundness shape to the cruciatedly interlacing holes. However semi-roundness shape needle was broken in the rat femur fracture fixation at week 4 to 6. The ideal design preserved enough window area and strong enough to fixate the fracture bone. The window area in 1/5 needle outer diameter design was about 3.6 square millimeters, just 0.8 times to that of $^1/_2$ needle outer diameter design, but the strength was enforced significantly. The cruciatedly interlacing holes design was 18 holes interlacingly arranged in the middle site of the needle. Holes diameter was 0.5 mm. 18 holes distributed at needle surface with length of 10 mm. So sum area of total 18 holes was 3.53 square millimeters, it was closed to 1/5 needle outer diameter design. FEA results showed that both middle site and lateral site bearing were largest in needle with $^1/_2$ outer diameter design, the needle with 1/5 outer diameter design was less but still more than the intact needle. The needle with cruciatedly interlacing holes design had almost no difference with the intact needle, and this design was our first choice. In fracture, lateral X-ray radiographs showed that Mg treated group showed 1.89 times callus area than the control group, its callus width was 1.38 times than the control at week 2. At week 4, Mg treated group had 1.64 times callus area than the control group, and the callus width was still 1.38 times than the control. At week 8, Mg treated group still had 1.71 times callus area than the control group, and the callus width was 1.4 times than the control. All the differences were vanished at week 12. CT results of fracture callus showed that Mg treated fracture bone group performed significantly more total callus bone volume than the control group at week 2, 4 and 8. At week 2, the total callus bone volume of Mg treated group was 1.178 times than that of control group. At week 4, the total callus bone volume of Mg treated bone was 1.417 times than the control group. At week 8, the Mg treated group still had 1.318 times than the control. We observed that the callus total volume in Mg treated group was remarkably higher than the control group from beginning to the end, and the increasing range was achieved to the top at week 4, after week 4, the increasing amount was sloping to a low value at week 8. Also all the differences were disappeared at week 12. At week 12, we carried biomechanical test, the results showed that Mg treated fracture femur had better bending resisting strength than the control (about 27% improvement to the control).
Discussion: FEA analysis helped us choosing a most appropriate needle design to fixate rat fracture bone and carrying Mg. We successfully applied Mg to treat fracture healing by a novel needle. X-ray and micro-CT results suggested the Mg containing needle significantly enhanced fracture callus volume. Biomechanical testing results proved Mg containing needle had excellent performance in fracture healing. This work firstly designed a hollow needle which carried Mg in treatment of fracture repair, and made Mg's orthopedic usage to be an applicable real in clinical field.
Conclusion: Data were presented as mean ± standard deviation. A two-sided, non-paired t test was used to analyze all the data, differences were considered significant as $p < 0.05$.
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HYDROTHERMALLY CONVERTED MARINE CORAL SCAFFOLD PROMOTES SEGMENTAL BONE DEFECT HEALING IN RATS

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Objective: Large segmental bony defects remain tough problems in clinical setting. Concentrated efforts have being made to develop different materials that can mimic both function and structure of natural bone tissue. Bone tissue engineering approaches are becoming more effective alternatives to autologous or allogenic bone grafting in the orthopedic surgery. Marine coral showed great potential as bio-scaffolds for their biomimetic composition and structure. Physical or chemical fabrication can reduce their immunogenicity and increase the mechanical strength. This study aims to investigate the effects of hydrothermal converted coral biomaterials on cell viability and bone regeneration *in vitro* and in *vivo*.
Methods: Hydroxyapatite nanopartical-coated and hydrothermal converted coral scaffolds were fabricated using established protocols. Natural coral and β-tricalcium phosphate (β-TCP) were taken as controls. Micro-computed tomography